

failure can be found in the fact that compared with other therapies the combination leads to a significant improvement in the clinical situation (higher cardiac ejection output and/or reversal of pulmonary congestion, and/or reversal of pulmonary wedge pressure, and/or a reduction in mortality caused by acute heart failure).

Example 19

Treatment with DPP-IV Inhibitor in Patients with Heart Failure

A DPP IV inhibitor according to the invention may be used to treat a patient with chronic heart failure. This treatment leads to a higher concentration of endogenous full length BNP (1-32) in vivo. The clinical efficacy of this treatment is tested in clinical studies. The treatment lasts between 2 weeks and 6 years. Evidence that the combination is effective in treating chronic heart failure can be found in the fact that a DPP-IV inhibitor according to the invention leads to a significant improvement in the clinical situation compared with a different treatment or placebo (less frequent hospitalisation due to acute heart failure, the ability to walk longer distances, a higher loadability in ergometrics, a higher cardiac ejection output and/or reversal of pulmonary congestion, and/or a reduction in mortality caused by heart failure).

What is claimed is:

1. A method of treating type 2 diabetes comprising administering to a patient in need thereof (a) 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine, or a therapeutically active salt thereof, in an oral dosage of 2.5 mg or 5 mg, and (b) metformin
wherein the dose of metformin is 100 mg to 500 mg or 200 mg to 850 mg (1-3 times a day), or 300 mg to 1000 mg once or twice a day, or as delayed-release metformin in a dose of 500 mg to 1000 mg once or twice a day, or 500 mg to 2000 mg once a day, or
wherein the dose of metformin is 500 mg, 850 mg or 1000 mg as a single dose with a total daily dose of metformin of 500-2850 mg, or 500 mg, 1000 mg, 1500 mg or 2000 mg metformin in delayed release form, or
wherein the dose of metformin is 500 mg to 1000 mg.
2. The method according to claim 1, wherein 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine and metformin are administered orally in the form of a fixed combination.
3. The method according to claim 2, wherein the fixed combination is a tablet or capsule.
4. The method according to claim 2, wherein the fixed combination is a tablet.
5. The method according to claim 2, wherein the dosage of 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine is 2.5 mg.
6. The method according to claim 2, wherein the dosage of 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine is 5 mg.
7. The method according to claim 2, wherein metformin is provided in a dose of 100 mg to 500 mg or 200 mg to 850 mg (1-3 times a day), or 300 mg to 1000 mg once or twice a day, or as delayed-release metformin in a dose of 500 mg to 1000 mg once or twice a day, or 500 mg to 2000 mg once a day.
8. The method according to claim 1, wherein the dose of metformin is 500 mg, 850 mg or 1000 mg as a single dose with a total daily dose of metformin of 500 mg to 2850 mg, or 500 mg, 1000 mg, 1500 mg or 2000 mg metformin in delayed release form.

9. The method according to claim 2, wherein the amount of metformin is 500 mg to 1000 mg.

10. The method according to claim 2, wherein the amount of metformin is 500 mg.

11. The method according to claim 2, wherein the amount of metformin is 850 mg.

12. The method according to claim 2, wherein the amount of metformin is 1000 mg.

13. A method of treating type 2 diabetes comprising administering twice daily to a patient in need thereof 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine in an oral dosage of 2.5 mg in fixed combination with metformin in an amount of 500 mg to 1000 mg.

14. An oral tablet formulation comprising 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine in an amount of 2.5 mg or 5 mg optionally in combination with metformin, and a pharmaceutically acceptable carrier or diluent.

15. The oral tablet according to claim 14, containing 500 mg to 1000 mg metformin.

16. A method of treating type 2 diabetes comprising administering to a patient in need thereof (a) 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine in a daily oral amount of 5 mg and (b) metformin, in the form of a fixed combination, wherein metformin is administered in a dose of 100 mg to 500 mg or 200 mg to 850 mg (1-3 times a day), or 300 mg to 1000 mg once or twice a day, or as delayed-release metformin in a dose of 500 mg to 1000 mg once or twice a day, or 500 mg to 2000 mg once a day.

17. A method of treating type 2 diabetes comprising administering to a patient in need thereof (a) 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine in a daily oral amount of 5 mg and (b) metformin, in the form of a fixed combination, wherein the dose of metformin is 500 mg, 850 mg or 1000 mg as a single dose with a total daily dose of metformin of 500-2850 mg, or 500 mg, 1000 mg, 1500 mg or 2000 mg metformin in delayed release form.

18. A method of treating type 2 diabetes comprising administering to a patient in need thereof (a) 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine in a daily oral amount of 5 mg and (b) metformin, in the form of a fixed combination, wherein the amount of metformin is 500 mg to 1000 mg.

19. The method according to claim 1, wherein 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine is administered in a daily oral amount of 5 mg.

20. A method of treating type 2 diabetes comprising administering to a patient in need thereof the oral tablet of claim 14, wherein the daily oral amount of 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine administered to said patient is 5 mg.

21. The method according to claim 5, wherein 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine in a dosage of 2.5 mg is administered twice daily.

22. The method according to claim 6, wherein 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine in a dosage of 5mg is administered once daily.